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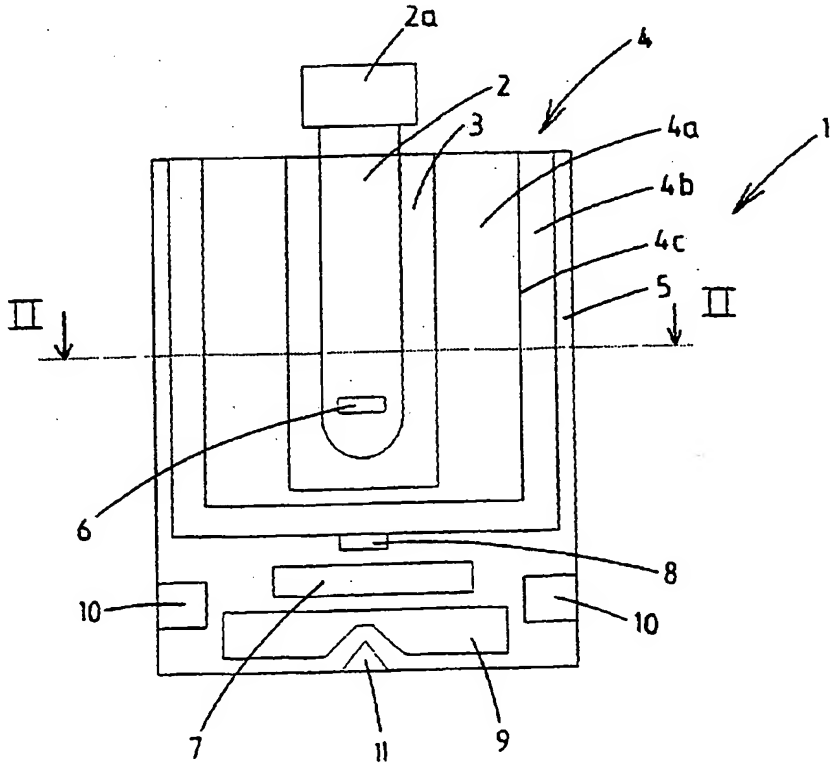
[Continued on next page]

(54) Title: ASSEMBLY OF AN INTEGRATED VESSEL TRANSPORTER AND AT LEAST ONE REACTION VESSEL, AND INTEGRATED VESSEL TRANSPORTER FOR TRANSPORTING A CHEMICAL SUBSTANCE



(57) Abstract: The invention comprises an assembly of an integrated vessel transporter (IVT) and at least one reaction vessel adapted to hold a chemical substance. The IVT is adapted to transport the vessel from a first station to a second station in an automated laboratory system. The IVT comprises conditioning means for conditioning at least one physical quantity of the substance. Further, the IVT comprises sensing means for sensing the at least one physical quantity. Still further, the conditioning means can be at least partly controlled by the sensing means. The conditioning means can comprise a stirrer, such as a contactless magnetic stirrer, and temperature conditioning means, comprising a heater and a heat sink. The temperature conditioning means can be controlled by a temperature sensor comprised in the stirrer.

WO 02/26386 A2

Assembly of an integrated vessel transporter and at least one reaction vessel, and integrated vessel transporter for transporting a chemical substance.

The invention relates to an assembly of an integrated vessel transporter (IVT) and at least one reaction vessel adapted to hold a chemical substance, the IVT being adapted to transport the vessel from a first station to a second station in an automated laboratory system. Further, the invention relates to an IVT for use in such assembly.

EP 0 916 406 A2 describes an IVT, indicated as a puck here, for holding a sample tube. The puck comprises a cylindrical housing and a tube-receiving opening at one end of the housing. To provide access to an interior space of the housing, the puck comprises an end cap at the opposite end of the housing. Further, the puck comprises a spring supported by the end cap, the spring having a plurality of arms projecting towards the tube receiving opening for holding a tube inserted in the opening.

IVT's or pucks as described above are used for transporting chemical substances comprised in a vessel, such as a sample tube, between stations in an automated laboratory system. In each station one or more specific operations are performed on the chemical substance comprised in the vessel. During transportation from station to station, as well as during waiting times in which the IVT is waiting to be processed by a station, such as when placed in a queue of IVT's, the IVT's, and also the chemical substances comprised in the vessels are exposed to environmental conditions. Commonly, these environmental conditions, as well as fluctuations therein, tend to deteriorate an accuracy of the experiments performed. A change in environmental conditions, such as temperature, humidity, atmospheric pressure and the like tends to adversely influence the accuracy of an experiment by the uncertainty in the environmental conditions, and by fluctuations in time during which a substance comprised in a vessel is subject to the environmental conditions, as transportation times and waiting times may differ for individual IVT's.

corrected as the conditioning means are at least partly controlled by the sensing means.

Advantageously, the conditioning means comprise a stirrer. The stirrer makes it possible to increase the homogeneity of the substance. In case that the substance comprises several constituents the homogeneity of the substance is increased by the stirring and thus, for example in case that a chemical reaction involving several constituents is taking place, changes or deviations in the chemical reaction by local differences in concentrations or temperatures of the constituents can be avoided.

Advantageously, the stirrer is arranged to be submerged in the substance and is arranged to be contactlessly driven by an alternating magnetic field, wherein advantageously the IVT comprises powering means for generating the magnetic field. This enables stirring the substance while causing minimum further, undesired interference on the substance, because no mechanical connection of the stirrer to any driving mechanism is required.

Advantageously, the stirrer comprises at least part of the sensing means. As the stirrer, which is submerged in the substance is in very close contact with the substance, placing at least part of the sensing means in the stirrer allows to perform measurements from within the substance. Thus, response time of the sensing means can be short, as any change in the physical quantity of the substance can be detected very quickly. Also, accuracy can be high, as the stirrer which comprises the sensing means is within the substance, causing a minimum of distance between the sensing means and the substance. Further, the sensing means can in this way detect an average of the physical quantity throughout the substance, as the stirrer is continuously moving through the substance making its stirring movement. A contactless stirrer comprising a sensing device has been described in unpublished EP 01201096.3, the text of which is incorporated herein by reference.

Advantageously, the conditioning means comprise temperature conditioning means. By conditioning temperature, a major factor causing changes in the substance comprised in the vessel can be largely eliminated.

Advantageously, the temperature conditioning means comprises a heat sink for cooling the substance. The heat sink provides a simple

comprises an electrical heater, thus providing further temperature stabilisation means in a simple and reliable manner.

Advantageously, the vessel is at least partly enclosed by the heater, which heater is at least partly enclosed by the heat sink. In this way, the temperature of the substance in the vessel can be very accurately stabilised making use of a push-pull like way of working, as the heater, which is in close proximity to the vessel is able to provide heat to the substance, while the heat sink enclosing the heater is able to remove heat from the substance, the heat sink (and outer enclosure) having been brought to an appropriate temperature. Further, a very quick response can be achieved, as, in case of an electrical heater, the heater very quickly responds to a change in electrical power supplied. Thus, a cooling by means of the heat sink, which is comparatively slow, can be combined with a fast (electrical) heater, enabling quick response, as an increase, a decrease, or a switch-off of power supplied to the heater will result in a fast heating respectively cooling of the substance comprised in the vessel. Further, as the heat sink at least partly encloses the heater and the vessel, environmental temperature changes will have little effect as the heat sink shields the vessel and heater from the environmental temperature.

Advantageously, the conditioning means comprise pressure stabilisation means. This allows to control (atmospheric) pressure in the vessel, for example in case that a reaction in the chemical substance produces gaseous substances or in case that the vessel comprises a volatile substance or in case that changes in atmospheric pressure might influence the accuracy of the experiment in any other way. The pressure stabilisation means can be implemented by means of a valve, a volume change means, an adding or removing of a gas, or in any other, suitable manner.

Advantageously, the IVT further comprises identification means for enabling the automated laboratory system to identify the IVT. Especially in automated laboratory systems which handle a significant amount of IVT's simultaneously or consecutively, identification of each IVT prevents errors by accidentally exchanging IVT's or wrongly identifying a puck. Also, in case of a breakdown or in case that a time period of transportation or performing an operation on the chemical substance in the vessel appears to be not exactly known,

comprise a rechargeable power source allowing for periodic recharging, such as for example in a station.

Advantageously, the power supply is positioned in a base portion of the puck, thus lowering a centre of gravity of the puck, and thus improving stability of the IVT while being transported.

Advantageously, the IVT comprises a locating feature, such as a protrusion or an indentation located in an exterior surface of the IVT for coupling the IVT to a transportation means. Making use of such locating feature, transportation of the IVT by the transportation means will be simplified, since the IVT can be taken in a predetermined position automatically.

Further, the invention comprises an IVT for use in an assembly according the invention.

Further advantages and features of the invention will be illustrated making use of the appended drawing showing a non-limiting embodiment, in which:

fig. 1 shows a schematic, cross-sectional side view of an assembly according to the invention; and

fig. 2 shows a cross sectional view of the assembly according to fig. 1.

Fig. 1 and 2 show an assembly of an IVT 1 and a vessel 2 such as a glass or metal vessel, in this example sealed by a stop 2a. The IVT 1 comprises a heater 3, such as an electric heater, which partly encloses the vessel 2. Further, the IVT 1 comprises a heat sink 4 placed around the heater 3. Further, the IVT 1 comprises an outer enclosure 5 surrounding the heat sink 4. The heat sink 4 comprises an inner part 4a which comprises a (solid) material having a high heat conductivity, and a buffer medium 4b. As shown in fig. 2, an interfacing surface area 4c between the inner part 4a and the buffer medium 4b is folded, in this example star shaped to increase the surface area. The IVT 1 further comprises an outer enclosure 5, and a stirrer 6, which is a contactless, magnetic stirrer for stirring a substance comprised in the vessel 2. The stirrer 6 is powered by powering means 7 generating a rotating magnetic field, thus causing the stirrer 6 to make a rotating movement in the vessel 2. The powering means 7 can for example comprise a plurality of electromagnetic coils which are provided with an electrical current in an alternating way to cause a rotating magnetic field.

temperature of the substance comprised in the vessel 2. Thus, the heat sink 4 attempts to decrease the temperature of the substance comprised in the vessel 2. The heater 3 however counteracts this decrease of temperature while providing heat to the substance in the vessel 2. The buffer medium 4b is brought to a desired temperature by conducting heat to or from the buffer medium 4b from the outer enclosure 5. During operation, the outer enclosure 5 is periodically brought to an appropriate temperature, which can for example be slightly lower than the temperature of the buffer medium 4b, causing a heating of the buffer medium 4b by the heater 3 or by the substance comprised in the vessel 2 to be counteracted by a cooling of the buffer medium 4b by the outer enclosure 5. Therefore, the outer enclosure 5 is preferably made of a material having a high thermal capacity, such as a granite. As the heater 3 is under control of the temperature sensor comprised in the stirrer 6 the amount of heat generated by the heater 3 can be accurately controlled by the control means (not shown) thus causing the temperature of the substance comprised in the vessel 2 to remain constant. As the vessel 2 comprising the substance is surrounded first by the heater 3, which is again surrounded by the heat sink 4, sensitivity for environmental temperature changes is low, as the vessel 2 is virtually shielded by the heat sink 4 for influences of an environmental temperature. Further, response time of the temperature conditioning means is short, as the response time of a heater, such as in this example an electrical heater is low, and as the heater 3 is in proximity of the vessel 2 and the substance comprised therein. Thus, sensing means data from the temperature sensor can be compared to a desired temperature by the control means and, if a deviation from the desired temperature is detected, the control means can control the amount of electrical power supplied to the heater 3, which instantaneously results in more or less or no (depending on the situation) heat generated by the heater and consequently in more or less or no heat received by the substance comprised in the vessel 2 from the heater 3.

In this manner, the assembly of the IVT 1 and the vessel 2 provide a transportation means for transporting a substance in an automated laboratory system, wherein the substance in the vessel can be stirred, and in which the temperature of the substance can be

CLAIMS

1. Assembly of an integrated vessel transporter (IVT) and at least one reaction vessel adapted to hold a chemical substance, the IVT being adapted to transport the vessel from a first station to a second station in an automated laboratory system, the IVT being characterised in that it comprises conditioning means for conditioning at least one physical quantity of the substance.

2. The assembly according to claim 1, characterised in that the assembly further comprises sensing means for sensing a parameter of the substance.

3. The assembly according to claim 2, characterised in that the conditioning means are at least partly controlled by the sensing means.

4. The assembly according to any of the preceding claims, characterised in that the conditioning means comprise a stirrer.

5. The assembly according to claim 4, characterised in that the stirrer is arranged to be submerged in the substance and is arranged to be contactlessly driven by an alternating magnetic field.

6. The assembly according to claim 5, characterised in that the IVT comprises powering means for generating the magnetic field.

7. The assembly according to any of claims 4 - 6, characterised in that the stirrer comprises at least part of the sensing means.

8. The assembly according to any of the preceding claims, characterised in that the conditioning means comprise temperature conditioning means.

9. The assembly according to claim 8, characterised in that the temperature conditioning means comprise a heat sink for cooling the substance.

transmitting sensing means data from the sensing means to a wireless receiver comprised in the IVT.

20. The assembly according to any of claims 2 - 19, characterised in that the sensing means comprise temperature sensing means.

21. The assembly according to any of claims 2 - 20, characterised in that the IVT further comprises logging means for logging sensing means data.

22. The assembly according to claim any of claims 2 - 21, characterised in that the IVT further comprises transmitting means for transmitting sensing means data and/or logged sensing means data to a remote receiver.

23. The assembly according to any of claims 2 - 22, characterised in that the IVT comprises a power supply for powering the conditioning means and/or the sensing means.

24. The assembly according to claim 23, characterised in that the power supply comprise a rechargeable power source.

25. The assembly according to claim 24, characterised in that the rechargeable power source comprises a capacitor.

26. The assembly according to any of claims 23 - 25, characterised in that the power supply is positioned in a base portion of the IVT.

27. The assembly according to any of the preceding claims, characterised by a locating feature, such as a protrusion or an indentation located in an exterior surface of the IVT for coupling the IVT to a transportation means.

28. IVT for use in an assembly according to any of the preceding claims.

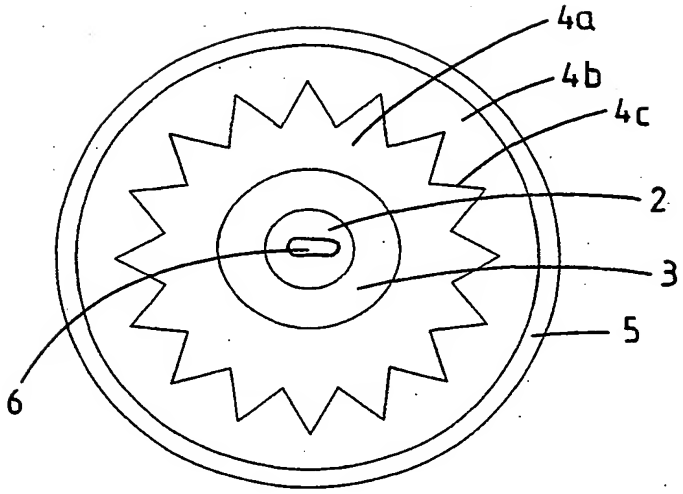


Fig. 2

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(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European

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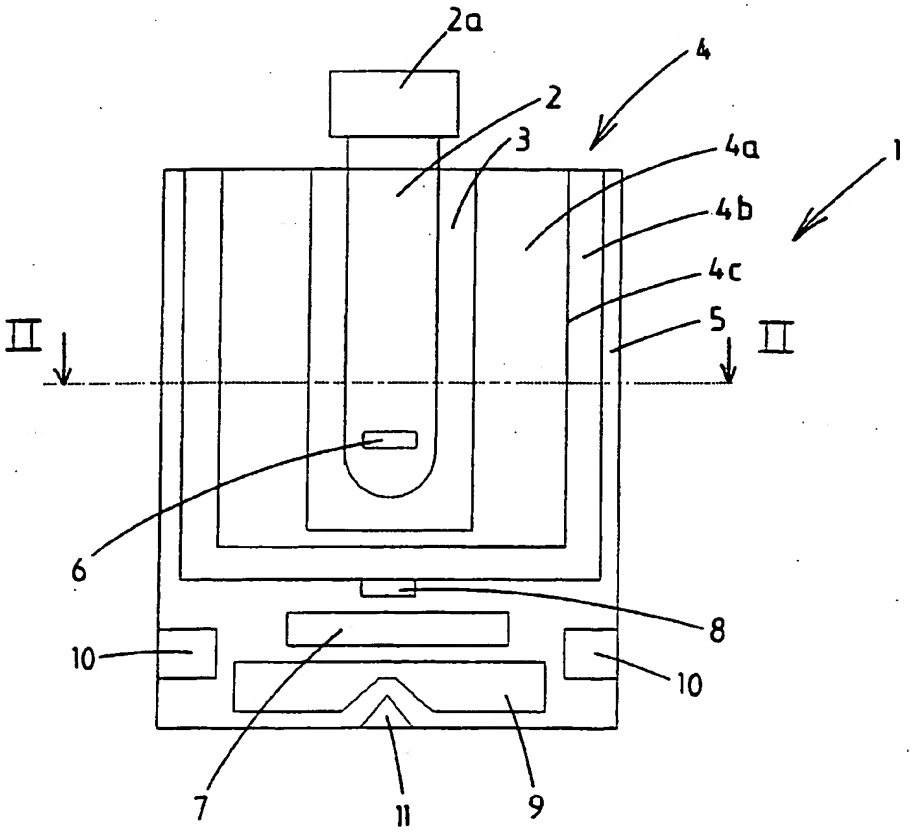

(57) Abstract: The invention comprises an assembly of an integrated vessel transporter (IVT) and at least one reaction vessel adapted to hold a chemical substance. The IVT is adapted to transport the vessel from a first station to a second station in an automated laboratory system. The IVT comprises conditioning means for conditioning at least one physical quantity of the substance. Further, the IVT comprises sensing means for sensing the at least one physical quantity. Still further, the conditioning means can be at least partly controlled by the sensing means. The conditioning means can comprise a stirrer, such as a contactless magnetic stirrer, and temperature conditioning means, comprising a heater and a heat sink. The temperature conditioning means can be controlled by a temperature sensor comprised in the stirrer.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01L3/00 B01L7/00 G01N35/04 B01L9/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N B01L B01F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 4 047 820 A (SOODAK CHARLES ET AL) 13 September 1977 (1977-09-13) abstract; figure 2 column 1, line 25 - line 26 column 2, line 31 - line 34 column 2, line 58 - line 66 ---	1,8,9, 14,28 18,27
Y	US 5 651 941 A (MAZZA JOHN ET AL) 29 July 1997 (1997-07-29) abstract; figure 2 column 3, line 12 -column 5, line 32 column 10, line 44 - line 60 column 13, line 4 - line 25 --- -/--	18,27

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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°&° document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 June 2002	26/06/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bockstahl, F

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Int...al Application No
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Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 4047820	A	13-09-1977	CA	1066917 A1	27-11-1979
			CA	1069341 A2	08-01-1980
US 5651941	A	29-07-1997	AU	665853 B2	18-01-1996
			AU	4537693 A	24-01-1994
			CA	2114527 A1	06-01-1994
			DE	69308493 D1	10-04-1997
			DE	69308493 T2	23-10-1997
			EP	0601173 A1	15-06-1994
			JP	6510233 T	17-11-1994
			WO	9400238 A1	06-01-1994
DE 4440250	A	15-05-1996	DE	4440250 A1	15-05-1996
EP 0916406	A	19-05-1999	US	5897090 A	27-04-1999
			EP	0916406 A2	19-05-1999
			JP	11218537 A	10-08-1999